

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Baldock, Sharon Claire
BOULT WADE TENNANT
Verulam Gardens
70 Gray's Inn Road
London WC1X 8BT
GRANDE BRETAGNE

MISS BALDOCK / NW
ADD RES 10/3/04
LD on Comp
In Date 2

PCT

INVITATION TO RESTRICT OR
TO PAY ADDITIONAL FEES

(PCT Rule 66)

Date of mailing
(day/month/year) 10.03.2004

Applicant's or agent's file reference
SCB/58858001

**REPLY OR
PAYMENT DUE** within 1 month(s)
from the above date of mailing

International application No.
PCT/GB 03/00034

International filing date (day/month/year)
07.01.2003

Priority date (day/month/year)
07.01.2002

International Patent Classification (IPC) or both national classification and IPC
C12Q1/68

Applicant
NORCHIP AS et al.

1. This International Examining Authority

- (i) considers that **the international application does not comply with the requirements of unity of invention** (Rule 13.1, 13.2 and 13.3) for the reasons indicated in the Annex.
- (ii) therefore considers that there are **5 inventions** claimed in the international application as indicated in the Annex.
- (iii) recalls that claims relating to inventions in respect of which no international search report has been established need not be the subject of international preliminary examination (Rule 66.1 (e)).

2. Consequently the applicant is hereby **invited**, within the time limit indicated above, **to restrict the claims** as suggested under item 3, below, **or to pay** the amount indicated below:

1530,00	x	4	=	6120,00
Fee per additional invention		number of additional inventions		total amount of additional fees

The applicant is informed that, according to Rule 68.3 (c), **the payment of any additional fee may be made under protest**, i.e. a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

- 3. **If the applicant opts to restrict the claims**, this Authority suggests the restriction possibilities indicated in the Annex, which in its opinion would be in compliance with the requirement of unity of invention.
- 4. **In the absence of any response** from the applicant, this Authority will establish the international preliminary examination report on those parts of the international application indicated in the Annex which, in the opinion of this Authority appear to relate to the main invention.

Name and mailing address of the international preliminary examining authority:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Aguilera, M

Tel. +31 70 340-385



**INVITATION TO RESTRICT
OR TO PAY ADDITIONAL FEES**

International application No. **PCT/GB03/00034**

The IPEA agrees with the objection put forward by the ISA as to lack of unity; the arguments presented in the annex to the Partial Search Report (Invitation to pay additional fees; form PCT/ISA/206) are fully maintained [see also PCT Preliminary Examination Guidelines 10.71-10.77]. Said arguments are hereby restated:

The common concept disclosed in the application can be considered as screening methods based on the detection of E6 mRNA.

However, this concept is not new in view of EP0373352 (BEHRINGWERKE AG; 20.06.1990), which discloses a method of detection of HPV E6 mRNA by RT-PCR (see Abstract and pages 2-5).

In view of this prior art, the problem to be solved by the present invention can be considered as providing further uses to the detection of HPV E6 mRNA. The solutions given by the present application are: (a) methods to assess and categorize the risk of developing cervical carcinoma; and (b) methods to screen for the presence of an integrated HPV or a modified episomal HPV genome.

Because no other technical features can be distinguished which, in view of the prior art could be regarded as special technical features in the sense of Rule 13.2 PCT, the IPEA is of the opinion that there is no single inventive concept underlying the plurality of claimed inventions of the present application in the sense of rule 13.1 PCT.

Consequently, there is a lack of unity, and the methods (a) and (b) are different groups of inventions not belonging to a common inventive concept.

Considering now the first group of inventions (a), the common concept can be considered as methods to assess the risk of developing cervical carcinoma based on the detection of HPV E6 mRNA.

However, this concept is not new in view of EP0373352 (see above), which also discloses the assessment of said risk by detecting the HPV E6 mRNA (see Abstract and page 2, lines 1-35).

In view of this prior art, the problem to be solved by the present invention can be considered as providing further methods to assess the risk of developing cervical carcinoma based on the detection of HPV E6 mRNA. The solutions given by the present application are the different combinations of marker mRNAs to be detected:

HPV E6 and HPV L1 mRNAs; HPV E6 and p16-INK4a mRNAs; or HPV E6 mRNA alone, excluding the detection of any other marker.

Because no other technical features can be distinguished which, in view of the prior art could be regarded as special technical features in the sense of Rule 13.2 PCT, the IPEA is of the opinion that there is no single inventive concept underlying the plurality of claimed inventions of the present application in the sense of rule 13.1 PCT.

Consequently, there is a lack of unity, and the methods and products claimed comprise different groups of inventions not belonging to a common inventive concept.

Considering now the second group of inventions above (b), the common concept can be considered as methods to screen for the presence of an integrated HPV or a modified episomal HPV genome by detecting HPV E6 mRNA.

However, this concept is not new in view of EP0373352 (see above), which also discloses that the detection of increased levels of HPV E6 mRNA performed by the method correlates with the integration event of HPV into the host cell genome (see page 2, lines 13-27. In general, the fact that E6 expression is up-regulated upon integration of HPV is well known since many years (see for example Durst et al., 1985; or Pater and Pater, 1985; both cited in page 16 of the description), and it cannot be considered to provide novel and inventive common concept for said methods.

In view of this prior art, the problem to be solved by the present invention can be considered as providing further methods to screen for the presence of an integrated HPV or a modified episomal HPV genome. The solutions given by the present application are the different combinations of marker mRNAs to be detected: HPV E6 and HPV L1 mRNAs; or HPV E6 mRNA alone, excluding the detection of any other marker.

Therefore, the following independent inventions have been identified in the present application which do not comply with the requirements of Rule 13.1 PCT:

Invention 1: Methods to assess the risk of developing cervical carcinoma based on the detection of E6 mRNA AND L1 mRNA. Kits to carry out said methods.
1, 2, 11-16 (all partially)

Invention 2: Methods to assess the risk of developing cervical carcinoma based on

**INVITATION TO RESTRICT
OR TO PAY ADDITIONAL FEES**

International application No. **PCT/GB03/00034**

the detection of E6 mRNA AND p16-INK4a mRNA. Kits to carry out said methods.
3 (complete); 11-16 (all partially)

Invention 3: Methods to assess the risk of developing cervical carcinoma based on the detection of E6 mRNA ALONE. Kits to carry out said methods.
6-10, 12-16 (all partially)

Invention 4: Methods of screening for the presence of integrated HPV based on the detection of HPV E6 mRNA AND L1 mRNA. Kits to carry out said methods.
4, 10-16 (all partially)

Invention 5: Methods of screening for the presence of integrated HPV based on the detection of HPV E6 mRNA ALONE. Kits to carry out said methods.
5, 8-10, 12-16 (all partially)

The applicant is hereby invited to pay additional fees for those inventions to be subject of International Preliminary Examination. **Since only Inventions 1 and 3 were subject of an International Search Report, the applicant is invited to pay one additional examination fee (Rule 66.1(e) PCT).** Should the applicant decide not to pay additional fees, the International Preliminary Examination will be restricted to Invention 1 as specified above [PCT Preliminary Examination Guidelines 10.75].